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Childhood adversity and chronicity of mood disorders

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Abstract To evaluate the potential impact of early childhood problems on the chronicity of mood disorders. A representative cohort from the population was prospectively studied from ages 19/20 to 39/40. Unipolar (UP) and bipolar disorders (BP) were operationally defined applying broad Zurich criteria for bipolarity. Chronicity required the presence of symptoms for more days than not over 2 years prior to an interview, or almost daily occurrence for 1 year. A family history and a history of childhood problems were taken at ages 27/28 and 29/30. Data include the first of multiple self-assessments with the Symptom-Checklist-90 R at age 19/20, and mastery and self-esteem assessed 1 year later. A factor analysis of childhood problems yielded two factors: family problems and conduct problems. Sexual trauma, which did not load on either factor, and conduct problems were unrelated to chronicity of UP or BP or both together. In contrast, childhood family problems increased the risk of chronicity by a factor of 1.7. An anxious personality in childhood and low self-esteem and mastery in early adulthood were also associated with chronicity. Childhood family problems are strong risk factors for the chronicity of mood disorders (UP and BP). The risk may be mediated partly by anxious personality traits, poor coping and low self-esteem.

Keywords Chronicity · Mood disorders · Childhood adversity · Coping · Self-esteem · Personality

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Introduction

There is growing evidence that early adversity plays an important role in the onset of mood disorders [1, 23, 24]. Numerous studies have documented associations between mood disorders and reports of parental indifference, over-control, and neglect, and physical and sexual abuse [19, 22, 31]. Although most of these data are retrospective, several prospective studies have also reported associations between childhood maltreatment and the later development of major depression [11, 38].

Our paper examines the relationship between childhood adversity and the course of mood disorders. The literature presents increasing evidence that childhood adversity impacts on the course of unipolar (UP) and bipolar (BP) mood disorders. It has been shown to correlate with an earlier onset and with higher recurrence/cycling of BP [14, 17, 25, 35] and UP [5]. Childhood adversity and maladaptive parenting were also found to be associated with chronic depression [9, 10, 28]. The association between childhood adversity and chronicity may be mediated by conduct disorder and shame-withdrawal in childhood [7], and, more importantly, by an increased vulnerability to stress in adulthood [15, 20, 39, 40]. However, in a small retrospective study comparing the relative impact of childhood adversity on the chronic course of UP and BP, Vocisano et al. [41] found that patients with chronic forms of UP and BP did not differ in terms of childhood maltreatment.

Recently, we reported that subjects with long-term/chronic as opposed to acute depression had an earlier age of onset and higher somatic and psychiatric comorbidity [4]. This paper extends our previous work by examining the link between childhood adversity and chronicity in mood disorders, and widens the scope of the earlier research by including bipolar depression.

Methodology

Zurich study

The design of the Zurich study was recently described in detail [2]. Essentially, it is a cohort study from ages 19/20 to 40/41 with six waves of interviews conducted by trained professionals. The interview sample ($N = 591$) was drawn from 4,547 subjects (2,201 males, 2,346 females) aged 19 (m) and 20 (f), who were representative of the canton of Zurich in Switzerland and screened in 1978 with the Symptom Checklist 90-R (SCL-90-R) [12]. The sample was stratified by high versus low scores on the General Severity Index of the SCL-90-R ("high risk" vs. "low risk" subjects), with oversampling of risk cases.

Over 20 years, the attrition rate was 38% (men 44%, women 31%). Only subjects participating in waves 3–6, i.e. at the ages of 27/28–40/41 (1986–1999), could be considered for the present analysis, because the temporal criteria for dysthymia had not yet been developed. The sample size is relatively small ($N = 499$) but, when sample stratification is statistically offset, it represents 2,146 subjects of the same age.

Chronic depression

There is no general agreement on the definition of long-standing, long-term, persistent or chronic depression [29]. The suggested minimum duration varies between 1 and 3 years [2]. In this study, a diagnosis of chronic major and minor depressive episodes required the temporal chronicity criterion for DSM-IV dysthymia (being symptomatic more days than not over 2 years), or mood changes had to be present almost daily over the 12 months prior to an interview; in both cases, work or social impairment had to be present.

Childhood and conduct problems

Childhood problems were assessed in retrospect at ages 27/28 and 29/30. The items are listed in Table 1.

Other variables

Unipolar depression and bipolar disorders were defined by the "broad" concept for bipolarity published earlier [3], which identified about half of all depressed subjects as bipolar. The concept is termed "broad" because it uses subthreshold definitions of hypomania and identifies more depressives as bipolar than the current DSM-IV concept. It requires a diagnosis of a major depressive episode according to DSM-IV and the presence of any number of the diagnostic symptoms of DSM-IV hypomania. No other criteria are

Table 1 Zurich study: factor analysis of childhood problems (tetrachoric correlations)

	Family problems	Conduct problems
Tense family atmosphere	0.77	−0.03
Sexual trauma	0.30	0.13
Broken home	0.61	0.14
Trouble with the police	−0.03	0.73
Restless in class	0.10	0.23
Unpunctual	0.05	0.71
Problems within family	0.81	0.21
Problems outside family	−0.09	−0.81
Father with psychol. problems	0.59	0.14
Mother with psychol. problems	0.44	0.18
Conflicts between parents	0.73	0.26
Conflicts with parents	0.61	0.24
Conflicts with other persons	0.81	−0.07
More punished than peers	0.49	0.38
Disliked, rejected by peers	0.50	0.36
Frequent physical fights	0.09	0.58
Discipline problems at school	0.09	0.78
Repeated running away	0.32	0.79
Theft	0.02	0.80
Truancy	0.19	0.86

Family problems are given in bold

Conduct problems are given in italics

applied. Psychiatric disorders were diagnosed by algorithms on the basis of DSM-III criteria (GAD, panic disorder), DSM-III-R criteria (major depressive disorder, phobias, obsessive–compulsive disorder (OCD)), and DSM-IV criteria (post-traumatic stress disorder and substance abuse/dependence). Mastery and self-esteem were assessed by the scales of Pearlin and Schooler [33] at age 20/21. Mastery means the extent to which individuals perceive their life-chances and/or outcomes as being under their own control rather than externally determined. Self-esteem refers to an individual's positive or negative attitude towards the self as a whole, and is assessed by statements such as "On the whole, I am satisfied with myself" and "I take a positive attitude towards myself". The Symptom Checklist 90 R (SCL-90-R) [13] was used for the self-assessment of depression, anxiety, somatisation and vegetative lability [36] at age 19/20. We present T-transformed scores (mean = 50, SD = 10). An anxious personality in childhood/adolescence refers to an individual's having been more anxious than his/her peers in childhood.

Statistics

Frequencies were compared across groups using χ^2 tests. Kruskal–Wallis tests were applied to continuous variables.

Apart from sample frequencies, we also report population estimates of cumulative incidence rates for a disorder. These are obtained as follows: first, the cumulative incidence rate of a disorder within the study sample is computed. The cumulative incidence rate is the percentage of subjects who *ever* reported (i.e. in any given interview) having had the disorder within the previous 12 months. It should be noted that, on account of the oversampling of risk cases, rates for most disorders are substantially higher in our sample than in the population. It should also be noted that the cumulative incidence rate is usually lower than the lifetime prevalence rate because it is based on the cumulation of (at most) 6–1-year prevalence rates. It can be considered as a lower bound for the lifetime prevalence rate. Moreover, the cumulative incidence rates in the sample are used to calculate population estimates using standard statistical procedures to offset sample stratification (i.e. to correct the bias introduced by oversampling risk cases). The results are cumulative incidence rates representative for the cohort of 19/20-year-olds in the population of the canton of Zurich in 1978.

The 20 dichotomous items on childhood adversity (Table 1) were factor analysed using a tetrachoric correlation matrix and oblique rotation. Eigenvalues, scree plot and results of Horn's parallel test were inspected to decide on the number of factors to be retained. The empirical and theoretical validity and interpretability of the factors were also considered in this decision.

A multivariate logistic regression was conducted to examine the influence of several predictors on the chronicity of mood disorder. The initial independent variables entered into the regression model were the level of childhood family problems, the level of childhood conduct problems, the presence of psychological problems in the father, the presence of psychological problems in the mother, the self-rating score of mastery (coping) at age 20/21, the self-rating score of self-esteem at age 20/21, the scores of the SCL scales for depression, anxiety, somatisation and interpersonal sensitivity at age 19/20 (t-transformed), the presence of an anxious personality in childhood/adolescence, the presence of a family history of depression, and the presence of a family history of mania or bipolar disorder. The models were reduced by eliminating, one by one, the least significant variable. If the deletion of a variable led to a change of more than 20% in one or more of the remaining regression coefficients, the variable was kept in the model. This procedure continued until only variables with a statistical significance level of at least $P < 0.1$ remained. Only these variables will be reported.

The overall analysis involved many tests of statistical significance, raising the problem of type I errors, i.e. of tests being statistically significant by chance alone. We offer a correction for multiple comparisons but nevertheless present the uncorrected *P*-values, because if only corrected values are shown, important findings may be missed. A Bonferroni-corrected threshold for statistical significance is reported with each table. The correction can be applied by simply raising the level of statistical significance to this threshold.

Analyses were performed in Stata 10.2 and SAS 8.2 for Windows.

Results

Descriptive data on the sample

We identified 104 major or minor bipolar (BP) subjects and 110 major or minor unipolar depressives (UP). The respective weighted cumulative incidence rates including the last interview (which are statistical estimates of the lower bound of population prevalence) were 15.4% (BP) and 14.8% (UP). There was no significant gender difference: 60.6% of BP (weighted 62.6%) and 60.0% of UP (weighted 61.4%) were women.

Thirty-eight BP subjects were chronic and 66 acute; among UP there were 43 chronic and 67 acute.

The 38 chronic BP subjects included 25 with MDE (67%), 14 of whom also met criteria for dysthymia. In all, 22 (58%) of the 38 chronic BP cases suffered from dysthymia. The remaining five non-dysthymic chronic cases suffered from recurrent brief depression ($N = 4$) and minor depression ($N = 1$).

The 43 chronic UP subjects consisted of 34 with MDE (79.1%), 21 of whom were also dysthymics. In all, 27 subjects (62.8%) with chronic UP were diagnosed as dysthymics. Of the remaining three non-dysthymic chronic UP cases, two suffered from recurrent brief depression and 1 from minor depression.

Factor analysis of childhood family problems

A factor analysis ($N = 397$) of the 20 items on childhood family problems resulted in two factors: family problems (F1) and conduct problems (F2; Table 1). The reliability (Cronbach's alpha) was 0.76 (F1) and 0.62 (F2). The two factors were uncorrelated ($r = 0.04$). Three items did not load strongly enough on the two factors and were excluded from the scales: "sexual trauma", "restless in class", and "problems outside the family". "Problems outside the family" loaded negatively on F2; this item was not included in the scale because its interpretation is uncertain and it does not fit with the other items representing conduct behaviour.

Childhood family and conduct problems by gender

The frequencies of childhood problems by gender are shown in Table 2. There were some differences: women reported more sexual trauma and psychological problems in their fathers and men reported more discipline problems at school and more trouble with the police.

There were no significant gender differences in family problems scores (F1) but, as expected, men scored significantly higher than women on behavioural/conduct problems (F2).

Childhood family and conduct problems in BP and UP subjects

UP and BP subjects did not differ in their total scores on the two factors: family problems (mean 3.2 ($s = 2.4$) vs. mean 3.1 ($s = 2.6$), $N = 82$ vs. 95) and conduct problems (mean 0.8 ($s = 1.4$) vs. mean 1.0 ($s = 1.4$), $N = 93$ vs. 100). At item level, being unpunctual at school was the only behaviour on which BP subjects scored higher. Sexual trauma did not differ significantly ($P < 0.21$) between the 110 UP (15.5%) versus 104 BP (22.1%) probands, but the two diagnostic groups differed significantly ($P < 0.0006$)

Table 2 Scores for childhood family and conduct problems ($M = 292$, $F = 299$)

	M	F	P
Tense family atmosphere	22.9	25.4	ns
Sexual trauma	4.8	18.7	0.001
Broken home	17.0	16.0	ns
Trouble with the police	41.4	15.4	0.001
Restless in class	27.6	21.6	ns
Unpunctual	8.9	4.3	0.05
Problems within family	42.2	47.8	ns
Problems outside family	0.4	1.3	ns
Father with psychol. problems	11.6	21.4	0.007
Mother with psychol. problems	17.1	23.7	ns
Conflicts between parents	25.8	29.5	ns
Conflicts with parents	28.1	24.8	ns
Conflicts with other persons	23.1	26.8	ns
More punished than peers	13.6	20.1	ns
Disliked, rejected by peers	12.4	18.1	ns
Frequent physical fights	8.0	6.9	ns
Discipline problems at school	20.4	8.6	0.001
Repeated running away	3.1	4.3	ns
Theft	14.2	8.2	0.04
Truancy	11.1	5.6	0.03

Family problems are given in bold

Conduct problems are given in italics

Bonferroni threshold: $P = 0.0025$

from the 183 other subjects without mood disorders (6.6%). In bipolar women, an interaction between the age of onset of hypomanic symptoms and a family history of depression was found with regard to the level of childhood family problems: in women with a family history of depression, the age of onset of their hypomanic symptoms rose from about 10 to 17 years with increasing levels of childhood family problems, but *decreased* from about 17 to 13 years in women without such a family history.

Childhood family and conduct problems in subjects with chronic versus acute BP and UP disorders

Table 3 presents the scores and significant differences between chronic and acute subgroups of mood disorders. Sufferers from chronic mood disorders scored consistently higher on childhood family problems; the differences were significant in the UP and in the combined (UP + BP) groups.

Interestingly, there were no associations between chronicity and the other variables entered into the analyses: sexual trauma, gender, SCL-90-R depression, anxiety and interpersonal sensitivity scores, family history of mania, and anxious personality (Table 3). Remarkably also childhood conduct problems were not associated significantly with chronicity (Table 4).

Multivariable logistic regression analyses on chronicity

Three multivariable logistic regression analyses were carried out comparing subjects with and without chronic UP, BP, and UP + BP.

Table 5 summarises the results. The score for childhood family problems was the most consistent predictor of chronicity across all three diagnostic groups with odds ratios between 1.7 and 1.8. Being more anxious than one's peers was a risk factor for UP (OR = 4.0) and for UP + BP (OR = 2.3). Unexpectedly, a family history of depression was negatively associated with chronic BP at a trend level (OR = 0.4) and with UP + BP (OR = 0.5). Furthermore, lower self-esteem was associated with chronic BP, as was decreased mastery in the merged group (UP + BP). Finally, somatisation, as measured by the SCL-90-R at age 19/20, was positively associated with chronic UP (OR = 2.1).

Discussion

Our data are restricted to a relatively small but representative age cohort interviewed four times from the ages of 27/28 to 39/40. The relatively small Ns may have created some type II errors. We must, therefore, also consider any

Table 3 Childhood problems and other characteristics of chronic versus acute mood disorders ($N = 397$)

	BP		P	UP		P	BP + UP		P	Oth.
	Chronic ($N = 38$)	Acute ($N = 66$)		Chronic ($N = 43$)	Acute ($N = 67$)		Chronic ($N = 81$)	Acute ($N = 133$)		$N = 183$
Female sex	57.9	62.1	0.67	55.8	62.7	0.47	56.8	62.4	0.42	41.0
Childhood family problems	3.8	2.8	0.08	3.9	2.7	0.05	3.8	2.7	0.008	1.6
Childhood conduct problems	0.8	1.0	0.53	0.9	0.7	0.35	0.8	0.9	0.88	0.4
Sexual trauma	23.7	21.2	0.77	20.9	11.9	0.20	22.2	16.5	0.30	6.6
Self-esteem (age 20)	13.1	14.6	0.02	13.8	13.6	0.46	13.5	14.1	0.22	14.7
Mastery/coping (age 20)	11.9	13.4	0.04	12.3	13.0	0.31	12.2	13.2	0.03	14.6
FH + depression	55.3	65.2	0.32	60.5	67.2	0.47	58.0	66.2	0.23	34.4
SCL depression (age 19)	67.5	64.9	0.27	67.5	65.7	0.28	67.5	65.3	0.11	58.4
SCL anxiety (age 19)	67.8	62.6	0.03	65.8	62.8	0.07	66.8	62.7	0.005	56.6
SCL somatization (age 19)	58.3	56.7	0.46	61.0	54.5	0.005	59.7	55.6	0.01	51.4
SCL interpers. sensitivity (age 19)	68.0	65.3	0.26	67.2	65.6	0.49	67.6	65.5	0.20	59.2
Anxious personality	33.3	23.4	0.29	35.0	17.0	0.05	34.2	20.5	0.03	15.7

Bonferroni threshold $P = 0.0014$

Table 4 Childhood conduct problems and chronicity

Conduct item	BP		UP		BP + UP	
	Chronic ($N = 38$)	Acute ($N = 66$)	Chronic ($N = 43$)	Acute ($N = 67$)	Chronic ($N = 81$)	Acute ($N = 133$)
Childhood conduct problems (mean)	0.8	1.0	0.9	0.7	0.84	0.86
Trouble with police (%)	26.3	28.8	30.2	26.9	28.4	27.8
Restless in class (%)	30.6	40.6	17.5	26.4	23.7	34.2
Unpunctual (%)	11.1	17.2	7.5	3.8	9.2	11.1
Frequent physical fights (%)	11.1	12.5	12.5	3.8	11.8	8.6
Discipline problems at school (%)	16.7	23.4	17.5	13.2	17.1	18.8
Repeated running away (%)	8.3	7.8	7.5	5.7	7.9	6.8
Theft (%)	14.1	8.3	15.0	15.1	11.8	14.5
Truancy (%)	13.9	17.2	17.5	11.3	15.8	14.5

Bonferroni threshold $P = 0.0019$

All P ns

Table 5 Predictors of chronicity: multivariable logistic regression

	BP		UP		BP + UP	
	OR	$P^{\dagger}$	OR	$P^{\dagger}$	OR	$P^{\dagger}$
Childhood family problems	1.8	0.02	1.7	0.05	1.7	0.002
Self-esteem (age 20)	0.5	0.01				
Mastery/coping (age 20)					0.7	0.03
FH + depression	0.4	0.08			0.5	0.04
SCL somatization (age 19)			2.1	0.01		
Anxious personality			4.0	0.02	2.3	0.03

Bonferroni threshold $P = 0.0028$

† Chronic versus acute

statistically significant trends in two of the three comparisons across the three groups: UP, BP, UP + BP. Unsurprisingly, we found two very distinct factors: childhood family problems and conduct problems.

The main positive finding of our study is the consistently strong (1.7-fold) elevation of risk for chronic mood disorders in subjects with childhood family problems. Prospective studies have reported an association between childhood adversity and adult depression [11, 37], but to our knowledge, none has investigated the relationship between early adversity and chronicity of adult mood disorders. A large patient study on dysthymia and double depression by McCullough et al. [30] found no differences

in early adversity between subgroups of chronic depression (major depression, dysthymia, double depression etc.). A smaller patient study by Vocisano et al. [41] reported that chronic UP and BP patients did not differ as regards childhood maltreatment. Our findings extend these studies and suggest that in the community childhood adversity is associated with chronicity of both UP and BP disorders. Finally, the findings that childhood/adolescent anxious personality, low self-esteem, and poor mastery were all associated with chronicity raise the possibility that the latter two factors may be expressions of early trait anxiety, and that all three may mediate the association between early adversity and chronic mood disorder.

In the multivariable analysis, the SCL-90-R (self-assessment) score for anxiety was not significantly associated with chronicity, in contrast to a self-described anxious personality in childhood and adolescence. And a positive family history of depression not only failed to predict but was negatively associated with chronicity, meaning that there were higher positive family history rates in the acute types of mood disorders, as was found for schizophrenia by Bleuler [6].

There were no differences on conduct problem scores between UP and BP subjects or between acute and chronic subtypes of mood disorders, although the expected gender difference [34] was present. These negative findings regarding conduct problems may be surprising; BP subjects might have intuitively been expected to score higher than their UP counterparts. On the other hand, one has to consider that clear mania in childhood is extremely rare. As the excellent Canadian follow-up study of high risk children of parents with BP conducted over 15 years, bipolar disorder was not observed before the age of 12 [16] and in 80% of cases manifested first as depression.

All three diagnostic groups (BP/UP/BP + UP) differed clearly from the residual group without mood disorders in potential risk factors for chronicity (Table 3, statistics not shown)—i.e. family history of depression, female gender, higher scores on childhood family and conduct problems, lower self-esteem and mastery, higher rates of anxious personality, and higher scores on the SCL-90-R scales for anxiety, depression, somatisation and interpersonal sensitivity. The findings regarding anxious personality are reminiscent of the results of the prospective Christchurch Health and Development Study, which found anxious and withdrawn behaviours to be predictive of later anxiety and mood disorders [18] and there is epidemiological confirmation of the familial risks of anxiety [26]. Although we found a number of clear risk factors, most of the variables did not significantly distinguish between the chronic and acute subtypes of mood disorders.

Among the strengths of the study is that it is based on a representative sample, repeatedly assessed prospectively over 20 years. It is limited, however, by the fact that the childhood variables were assessed retrospectively 15–20 years after the event. Although findings from retrospective studies must be regarded cautiously [21], depressed persons' reports of childhood adversity are stable despite changes in clinical state and over periods of up to 20 years [27, 42]. In addition, adults' retrospective reports of childhood adversity are often corroborated by informants or records [8, 21] and several prospective studies have reported associations between childhood maltreatment and later mood disorders [11, 37]. Furthermore, twin studies indicate that genetic factors cannot explain the association between early adversity and mood disorders [32].

Finally, we have performed many tests of statistical significance, raising the problem of type I errors (false positive tests). Our approach to this issue was to offer a correction for multiple comparisons but nevertheless to present the uncorrected P-values so that potentially important findings are not obscured by the correction.

Conclusion

Childhood family problems were strongly associated with chronicity of both bipolar and unipolar mood disorders. Our data are also in line with the hypothesis that childhood adversity may create a vulnerability in the form of childhood anxious personality and low self-esteem and mastery that predispose to chronic mood disorders. However, this requires further analysis and confirmation by other studies.

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